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Reactivity of 3-Substituted Indolin-2-ones in Vilsmeier-type Reactions of 4,6-Dimethoxyindoles

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Abstract:: 4,6-Dimethoxy-2,3-diphenylindole 1 undergoes reaction with the 3-substituted indolin-2ones 7,8,11-14 and either phosphoryl chloride or triflic anhydride to give the 2,7'-bindolyl 16, the 7,7'; 2,7'-terindolyls 19, 20 and the 7,7'-bindolyl 23. Copyright © 1996 Elsevier Science Ltd

Indolin-2-one and 4,6-dimethoxyindolin-2-one have been shown to undergo reaction with phosphoryl chloride and a range of indoles to yield the related 2-substituted indoles.^{1,2} In some cases, further reaction occurred at the unsubstituted 3-position of the 2-indolyl substituent to give terindolyl products. For example, 4,6-dimethoxy-2,3-diphenylindole 1 underwent reaction with indolin-2-one and 4,6-dimethoxyindolin-2-one in the presence of phosphoryl chloride to yield the 2,7'-biindolyls 2 and 3 respectively. Some of the terindolyl 4 was also formed in the latter reaction. In an attempt to control the regioselectivity of reaction of the 2,7'biindolyl 3, formylation of it was investigated. Reactions involving one equivalent of phosphoryl chloride in dimethylformamide at 0 °C led to complex mixtures. The use of excess phosphoryl chloride gave better results, but extensive chromatography was still required for product isolation. The use of trifluoromethanesulfonic (triflic) anhydride instead of phosphoryl chloride gave similar results. Formylation at C7 could not be achieved because of preferential reaction at C3, leading ultimately to the fully unsaturated product 6, after the processes of cyclisation and dehydration had occurred. Similar behaviour was observed with the 2,7'-biindolyl 2, which afforded the related product 5. Both bright orange-yellow compounds 5 and 6 were relatively insoluble and difficult to purify, and satisfactory analytical data could not be obtained. However, their structures were established by spectroscopic data. In particular, there were neither carbonyl nor NH stretching frequencies in the infrared spectra, nor were there appropriate aldehyde or NH resonances in the ¹H n.m.r. spectra. Mass spectroscopic data were consistent with the proposed structures. In order to overcome the general problem of substitution at C3, the reactivity of 3-substituted indolin-2-ones in the modified Vilsmeier reaction was investigated. The choice of 3-substituted indolin-2-ones was based on several premises. 3-Methylindolin-2-one 7³ and the related dithiolan 8⁴ represent model compounds, which would respectively allow the C3 substituent to remain or be removed subsequently by treatment with Raney nickel.⁵ In view of the need to continue to functionalise the initial products at C7, 4,6-dimethoxy activation was also desired. Consequently the previously unknown indolin-2-ones 11, 13 and 14 were prepared from 4.6-dimethoxyisatin 9, which in turn was derived from 3,5-dimethoxyaniline hydrochloride and oxalyl chloride.^{6,7} 4,6-Dimethoxyisatin 9 was reacted initially with phenyl lithium in tetrahydrofuran to produce the dioxindole 10, which was reduced by stannous chloride in acetic acid to produce the 3-phenylindolin-2-one 11. Similarly, isatin 9 was reacted with methylmagnesium chloride to produce the dioxindole 12, which was converted to the 3-methylindolin-2-one 13. Furthermore, isatin 9 was reacted with ethane-1,2-dithiol and boron trifluoride etherate in acetic acid to produce the spiro compound 14. In an alternative approach, the 2-bromoanilide 15, prepared from 4,6-dimethoxyaniline and 2-bromopropanoyl chloride, could not be cyclised to give the indolin-2-one 13.



Initially it was found that the reaction between 4,6-dimethoxy-2,3-diphenylindole 1 and 3methylindolin-2-one 7 with phosphoryl chloride produced the 2,7'-biindolyl 16 in 71% yield, together with a trace of 2-chloro-3-methylindole 17. The fact that the latter compound 17 was detected shows that it is somewhat reluctant to undergo further reaction, because of the presence of the 3-methyl group. Under similar conditions the spiro-indolin-2-one 8 proved to be unreactive and after 12 hours reflux, the only observed product was the 7,7'-biindolyl 18. This compound clearly arises from the oxidative dimerisation of the indole 1, and has been observed in trace amounts in similar previous reactions. It has been synthesised quantitatively by the oxidative dimerisation of indole 1 using either a variety of quinones or iodine monochloride.^{8,9}

Indolin-2-ones 11 and 13 were each reacted with indole 1 and phosphoryl chloride and predominantly formed the 7,7'; 2,7'-terindolyl compounds 19 (45%) and 20 (38%) respectively. Clearly the indolin-2-ones 11 and 13 underwent initial reaction with indole 1 to produce the desired 2,7'-bi-indolyl system, which then combined with a further equivalent of indole 1. Once again in each reaction the formation of small amounts of the 7,7'-biindolyl 18 was observed. Although it could be seen from ¹H n.m.r. spectra of partially purified reaction mixtures that traces of quater- and poly-indolyl systems were also produced, the only other product that could be isolated was the 2,2'-bi-indolyl 21 in a 5% yield from the reaction of indolin-2-one 11. The isolation of this 2,2'-bi-indolyl 21 would seem to indicate that the intermediate 2-chloroindole resulting from the reaction of indolin-2-one 11 and phosphoryl chloride undergoes a coupling reaction of some type.



Therefore, this would substantiate the hypothesis that the phosphoryl chloride in these reactions could chlorinate indole 1 at C7 to give a product which then could undergo a similar kind of coupling. Furthermore, terindolyls 19 and 20 could then be obtained by the same type of reaction. Replacement of phosphoryl chloride with triflic anhydride led to cleaner reactions and higher yields of the terindolyls 19 and 20 (60% and 50% respectively). Again, small amounts of the 7,7'-biindolyl 18 were observed.

In contrast to the spiro-indolin-2-one 8, the dimethoxy analog 14 did react with indole 1 and phosphoryl chloride, demonstrating the activating influence of those groups. However, the product was not the expected 2,7'-biindolyl 22, but a 7,7'-biindolyl type of compound, which was shown to have the unusual structure 23. A trace of the 7,7'-biindolyl 18 was also observed in this reaction.

The structure of compound 23 was elucidated from ¹H and ¹³C n.m.r. spectroscopic data. The ¹H n.m.r. spectrum showed two distinct signals near 10.3 ppm corresponding to two NH resonances which both disappeared during a D₂O exchange experiment. Also there were two distinct singlets near 6.4 ppm corresponding to H6 and H5' (note carbazole numbering). If the expected product 22 had been formed, the spectrum should contain only one NH signal, a singlet for H5' at ~6.0 ppm and a set of two meta coupled doublets for H5 and H7 at 6.0–6.5 ppm. The ¹³C n.m.r. spectrum also indicates two CH signals at 90.6 and 89.6 ppm which corresponding to C5' of structure 23. Again if product 22 were formed, three CH signals at ~90 ppm corresponding to C5', C5 and C7 would be expected. Also the characteristic C3 spiro carbon signal, which is usually located at 60–65 ppm, is missing from the ¹³C n.m.r. spectrum. Furthermore, the infrared spectrum shows two clear resonances at 3463 and 3373 cm⁻¹ corresponding to two NH stretching frequencies.



Previously, it has been found that 1,3-dithiolanes formed on a carbon attached directly to an aromatic ring undergo a rapid, high-yield rearrangement to dihydro-1,4-dithiin derivatives, provided that a methyl or methylene group is available in the other α -position.^{10,11}

It is possible that the resulting intermediate from the reaction of indolin-2-one 14 with phosphoryl chloride could undergo a concerted rearrangement in the presence of acid to give a stabilized carbocation, which could then undergo nucleophilic attack from indole 1 followed by aromatization to give compound 23. This rearrangement must occur reasonably quickly as the desired product 22 was not observed: such a hypothesis is consistent with previous reports^{10,11}.

The reaction of the spiro-indolin-2-one 14 with phosphoryl chloride on its own yielded no isolable products. After an extended period of reflux the reaction mixture contained multiple products in very small

yields. Similar behaviour was shown by the other 3-substituted indolin-2-ones 11 and 13 and contrasts with that shown by 4,6-dimethoxyindolin-2-one itself.²



EXPERIMENTAL

General Information

¹H n.m.r. spectra were recorded at 300 MHz with a Bruker CXP-300 or at 500 MHz with a Bruker AM-500 spectrometer, and refer to deuterochloroform solutions with chloroform (7.26 ppm) as an internal standard. Signals due to exchangeable protons (NH) were identified by exchange with deuterium oxide. The usual notational conventions are used. ¹³C n.m.r. spectra were recorded at 125.77 MHz with a Brucker AM-500 spectrometer, and refer to deuterochloroform solutions with chloroform (77.0 ppm) as an internal standards. Low resolution mass spectra were obtained on an A.E.I. MS12 spectrometer at 70eV and 8000V accelerating potential at 210 °C ion source temperature. Infrared spectra were recorded with a Perkin Elmer 580B and refer to paraffin mulls or KBr disks of solids. Ultraviolet spectra were measured using a Hitachi UV-3200 spectrophotometer. Microanalyses were performed by Dr. H.P. Pham of the UNSW Microanalytical Unit.

10,12-Dimethoxy-1,2-diphenylindolo[3,2-e]pyrrolo[3,2,1,-i,j]quinoline (5)

To a stirred and ice cooled solution of 2,7'-bi-indolyl 2 (0.2g, 0.45mmol) in dimethylformamide (2ml) was added dropwise an ice cold solution of phosphoryl chloride (0.16g, 0.10ml, 1.08mmol) in dimethylformamide (1ml). The solution was allowed to come to room temperature and then was made strongly basic with sodium hydroxide solution (20%). The resulting orange-yellow precipitate was collected, washed with water and dried. This solid was then column chromatographed using chloroform/methanol 9:1 as the eluent to give compound 5 (0.08g, 40%), m.p. 184-189 °C. ¹H n.m.r. (CDCl₃): δ 4.01 and 4.40, 2s, OMe; 6.83, s, H11;

7.28-7.53, m, 12H, ArH; 7.94, d, J8.1Hz, 1H, ArH; 8.15, d, J8.1Hz, 1H, ArH; 8.84, s, H4. Mass spectrum: *m/z* 454(M, 100%), 440(60), 439(50), 425(55), 409(20).

5,7,10,12-Tetramethoxy-1,2-diphenylindolo[3,2-e]pyrrolo[3,2,1,-i,j] quinoline (6)

In a similar manner to the synthesis of compound 5, 2,7'-bi-indolyl 3 (0.2g, 0.40mmol) gave the orangeyellow compound 6 (0.02g, 10%), m.p. 184-189 °C. ¹H n.m.r. (CDCl₃): δ 3.88, 3.92, 4.08 and 4.37, 4s, OMe; 6.60, 6.70 and 7.17, 3s, H5, H7, H11; 7.36, s, 5H, ArH; 7.57-7.62, m, 5H, ArH; 8.95, s, H4. Mass spectrum: m/z 514(M, 75%), 515(100), 499(39), 498(38), 431(58).

4,6-Dimethoxyisatin (9)

3,5-Dimethoxyaniline hydrochloride (17g, 0.09mol) was thoroughly mixed with oxalyl chloride (17ml, 0.2mol) in a 500 ml open flask and heated to 165-170 °C for 1h. On cooling methanol was added and the mixture refluxed and filtered while hot. The resulting dark green solid was dissolved in a 5% sodium hydroxide solution and left to stand for 5 min. The dark red solution obtained was then acidified to pH4 with formic acid and left to stand for 1h. The resulting brown yellow precipitate was then collected, washed with water and dried. This solid was then placed into a Soxhlet thimble and extracted with dichloromethane over a period of two weeks to give the isatin as a bright yellow solid (14.9g, 80%), m.p. 296-299 °C, (lit⁷ m.p. 292-295 °C).

4,6-Dimethoxy-3-hydroxy-3-phenylindolin-2-one (10)

Phenyl lithium (10ml, 20%) was added to a stirred and ice cooled solution of isatin 9 (5g, 24.0mmol) in anhydrous tetrahydrofuran (250ml). The mixture was brought to room temperature for 20 min then neutralised with a solution of ammonium chloride. The product was separated using dichloromethane and evaporated to dryness. Dichloromethane was added and the mixture refluxed and filtered while hot to afford the product 10 as a white solid (5.6g, 81%), m.p. 206-208 °C. (Found: C, 67.4; H, 5.2; N, 4.9. C₁₆H₁₅NO₄ requires C, 67.4; H, 5.3; N, 4.9%). λ_{max} 230nm(ε 18660), 284(2120). ν_{max} 3420, 3171, 2924, 1714, 1635, 1518, 1471, 1359, 1315, 1230, 1153, 989, 893, 844, 800 cm⁻¹. ¹H n.m.r. [(CD₃)₂SO]: δ 3.41, bs, OH; 3.58 and 3.77, 2s, OMe; 6.13, d, J2.0Hz, H5; 6.17, d, J2.0Hz, H7; 7.19-7.28, m, ArH; 10.28, bs, NH. ¹³C n.m.r. [(CD₃)₂SO]: δ 55.55 and 55.69, OMe; 89.71 and 92.71, C5 and C7; 125.81, 127.33 and 128.02, ArCH; 77.47, C3; 111.13, C3a; 141.16, C1'; 144.43, C7a; 157.47 and 162.40, <u>C</u>-OMe; 179.17, C=O. Mass spectrum: *m*/z 285(M, 65%), 269(75), 256(100), 240(35), 180(25).

4,6-Dimethoxy-3-phenylindolin-2-one (11)

Stannous chloride (3.79g, 20mmol) in acetic acid (100ml) and hydrochloric acid (10ml) were added to a solution of dioxindole **10** (5.0g, 17.5mmol) in acetic acid (20ml) and heated to 80-90 °C for 0.5h. The solution was then poured into ice water, the resulting white precipitate collected and dried. The crude product was placed in a Soxhlet thimble, extracted with dichloromethane and evaporated to dryness to give a white solid (4.6g, 98%), m.p. 236-238 °C. (Found: C, 71.4; H, 5.6; N, 5.2. C₁₆H₁₅NO₃ requires C, 71.4; H, 5.6; N, 5.2%). λ_{max} 224nm (ε 24800), 262(2790). v_{max} 3158, 1709, 1605, 1452, 1348, 1149, 1112, 814, 709 cm⁻¹. ¹H n.m.r. [(CD₃)₂SO]: δ 3.59 and 3.77, 2s, OMe; 4.53, s, H3; 6.17, d, J2.0Hz, H5; 6.21, d, J2.1Hz, H7; 7.07-7.46, m, ArH; 10.41, s, NH. ¹³C n.m.r. [(CD₃)₂SO]: δ 50.20, CH; 55.55 and 55.64, OMe; 89.55 and 92.44, C5 and C7; 127.06, 128.11 and 128.59, ArCH; 107.41, C3a; 137.56, C1'; 144.98, C7a; 156.61 and 161.66, <u>C</u>-OMe; 177.83, C=O. Mass spectrum : m/z 270(M+1, 15%), 269(M, 100), 254(50), 240(40).

4,6-Dimethoxy-3-hydroxy-3-methylindolin-2-one (12)

Methyl magnesium chloride (3ml, 20% solution) was added to a stirred and ice cooled solution of isatin 9 (1.0g, 4.8mmol) in dry tetrahydrofuran (50ml). The mixture was brought to room temperature for 20 min then neutralized with a solution of ammonium chloride. The product was separated using dichloromethane and recrystallised from dichloromethane and petroleum ether to give the dioxindole 12 as a pale cream solid (0.8g, 74%), m.p. 195-198 °C. (Found: C, 59.4; H, 5.9; N, 6.5. C₁₁H₁₃N0₄ requires C, 59.2; H, 5.9; N, 6.3%). λ_{max} 224nm (ϵ 24957), 266 (2456). ν_{max} 3275, 3223, 1712, 1631, 1611, 1520, 1368, 1345, 1234, 1159, 819 cm⁻¹. ¹H n.m.r. [(CD₃)₂SO]: δ 1.39, s, Me; 3.73 and 3.76, 2s, OMe; 5.48, s, OH; 6.00, d, J2.1Hz, H5; 6.14, d, J2.0Hz, H7; 10.08, s, NH. ¹³C n.m.r. [(CD₃)₂SO]: δ 22.53, Me; 55.59 and 55.65, OMe; 89.65 and 82.39, C5 and C7; 72.93, C3; 111.07, C3a; 143.60, C7a; 157.71 and 161.95, <u>C</u>-OMe; 180.42, C=O. Mass spectrum : *m*/z 223(M, 38%): 208(100), 180(70).

4,6-Dimethoxy-3-methylindolin-2-one (13)

Stannous chloride (1.0g, 4.4mmol) in acetic acid (20ml) and hydrochloric acid (1ml) was added to a solution of dioxindole (48) (0.5g, 2.2mmol) in acetic acid (10ml) and heated to 80-90 °C for 0.5h. The solution was cooled and the product separated using dichloromethane and recrystallised from dichloromethane and petroleum ether to give the indolin-2-one **13** as a pale cream solid (0.39g, 85%), m.p. 135-137 °C. (Found: C, 63.9; H, 6.4; N, 7.0. $C_{11}H_{13}NO_3$ requires C, 63.8; H, 6.3; N, 6.8%). λ_{max} 231nm(ϵ 10129), 256(3607). ν_{max} 3136, 3060, 1710, 1639, 1619, 1597, 1522, 1220, 1207, 1154, 1120, 810, cm⁻¹. ¹H n.m.r. (CDCl₃): δ 1.49, d, J7.6Hz, Me; 3.45, q, J7.6Hz, H3; 3.78 and 3.80, 2s, OMe; 6.14, d, J2.1Hz, H5; 6.17, d, J2.0Hz, H7; 9.13, s, NH. ¹³C n.m.r. (CDCl₃): δ 14.41, Me; 39.89, CH; 55.18 and 55.54, OMe; 89.24 and 92.66, C5 and C7; 109.51, C3a; 143.04, C7a; 156.66 and 161.26, <u>C</u>-OMe; 163.08, C=O. Mass spectrum: *m/z* 207(M, 60%), 192(100).

4,6-Dimethoxy-3-spiro(1',3'-dithiolan-2'-indolin)2-one (14)

To a solution of isatin **9** (2.07g 0.01mol) in acetic acid (60ml) at 60 °C was added ethane-1,2-dithiol (1ml, 0.01mol) followed by slow addition of boron trifluoride etherate (2ml, 0.02 mol). The solution was kept at 60 °C for 20 min then cooled, water added, and the resulting pale brown precipitate filtered off and washed with water to give the indolin-2-one **14** (3.4g, 80%), m.p. 228 °C (from ethyl acetate). (Found: C, 50.7; H, 4.6; N, 5.2. C₁₂H₁₃NO₃S₂ requires C, 50.9; H, 4.6; N, 4.9%). λ_{max} 237nm (ϵ 21388), 290(3241). ν_{max} 3143, 3062, 1716, 1619, 1517, 1345, 1281, 1204, 1159, 1121, 811 cm⁻¹. ¹H n.m.r. [(CD₃)₂SO]: δ 3.63, m, CH₂; 3.75 and 3.79, 2s, OMe; 6.04, d, J2.1Hz, H5; 6.19, d, J2.1Hz, H7; 10.50, bs, NH. ¹³C n.m.r. [(CD₃)₂SO]: δ 40.07, CH₂; 55.78 and 56.00, OMe; 89.73 and 93.04, C5 and C7; 62.13, C3; 104.87, C3a; 143.39, C7a; 157.55 and 162.72, <u>C</u>-OMe; 178.98, C=O. Mass spectrum: *m*/z 283(M, 85%), 255(65), 244(50), 223(100), 222(80), 194(55).

N-(3,5-Dimethoxyphenyl)-2-bromopropanamide (15)

2-Bromopropanoyl chloride (0.7ml, 6.6mmol) in dry tetrahydrofuran (5ml) was added dropwise to a stirred and ice-cooled solution of 3,5-dimethoxyaniline (1.01g, 6.6mmol) and dry pyridine (0.54ml, 6.6mmol) in dry tetrahydrofuran (20ml). The solution was brought to room temperature and stirred for 1h. The solution was then evaporated to dryness and the product separated from the crude mixture by column chromatography using dichloromethane as eluent to give the product 15 (1.23g, 65%), m.p. 81-82 °C (from dichloromethane and petroleum ether). (Found: C, 46.2; H, 5.2; N, 4.8. C₁₁H₁₄BrN0₃ requires C, 45.9; H, 4.9; N,4.9%). λ_{max} 264nm(ε 8139). ν_{max} 3286, 3232, 3175, 3120, 1671, 1631, 1610, 1568, 1209, 1072 cm⁻¹. ¹H n.m.r. (CDC1₃): δ 1.91, d, J7.0Hz, Me; 3.75, s, OMe; 4.51, q, J7.0HZ, H2; 6.24, t, J2.3Hz, 1H, ArH; 6.77, d, J2.2Hz, 2H, ArH; 8.22, s, NH. ¹³C n.m.r. (CDCl₃): δ 22.37, Me; 44.60, CH; 55.29, OMe; 97.35 and 98.39, ArCH; 138.67, ArC; 160.94, <u>C</u>-OMe; 167.87, C=O. Mass spectrum: *m/z* 289(M, ⁸¹Br, 41%), 287(M, ⁷⁹Br, 39%), 208(100), 180(45), 153(35).

General procedure for the reaction of indole 1 with either phosphoryl chloride or triflic anhydride

To a stirred solution of indole 1 (1.52mmol) and an indolin-2-one (1.52mmol) in anhydrous chloroform (30ml) was added either phosphoryl chloride or triflic anhydride (3.04mmol). After either refluxing for 4-12h, or stirring for 30 min at room temperature respectively, the mixture was cooled and made strongly basic with sodium hydroxide solution (10%). The mixture was extracted with chloroform, dried, concentrated and chromatographed on silica gel using dichloromethane as the eluent to yield the product.

Reaction of indole 1 and indolin-2-one 7 with phosphoryl chloride

Indole 1 (0.5g, 1.52mmol) and indolin-2-one 7 (0.23g, 1.52mmol) gave two products.

(i) 4.6-Dimethoxy-7-(3'-methylindol-2'-yl)-2,3-diphenylindole (16)

(0.49g, 71%), Rf 0.65, m.p. 215 °C (from dichloromethane and petroleum ether). (Found: C, 81.2; H, 5.5; N, 6.1. C₃₁H₂₆N₂O₂ requires C, 81.2; H, 5.7; N, 6.1%). λ_{max} 245nm(ε 21743), 319(15140). ν_{max} 3440, 3422, 3405, 1624, 1607, 1340, 1140, 749 cm⁻¹. ¹H n.m.r. [(CD₃)₂SO]: δ 2.15, s, Me; 3.72 and 3.79, 2s, OMe; 6.51, s, H5; 6.98-7.52, m, ArH; 10.72, s, NH; 10.80, s, NH. Mass spectrum: *m*/z 459(M+1, 38%), 458(M, 100%), 443(45), 329(15), 229(15).

(ii) 2-Chloro-3-methylindole (17)

(0.007g, 1%), R_f 0.75, m.p. 125 °C (from dichloromethane and petroleum ether). ¹H n.m.r. [(CD₃)₂SO]: δ 2.19, s, Me; 7.02, t, J7.5Hz, 1H, ArH; 7.10, t, J7.6Hz, 1H, ArH; 7.27, d, J8.1Hz, 1H, ArH; 7.43, d, J7.9Hz, 1H, ArH; 11.55, s, NH. Mass spectrum: m/z 167(M, ³⁷Cl, 30%), 166(40), 165(M, ³⁵Cl, 100%), 164(95), 140(80), 138(40).

Reaction of indole 1 and indolin-2-one 11 with phosphoryl chloride

Indole 1 (0.5g, 1.52mmol) and indolin-2-one 11 (0.41g, 1.53mmol) gave two products.

(*i*) 4,6-Dimethoxy-7-[4',6'-dimethoxy-3'-phenyl-7'-(4'',6''-dimethoxy-2'',3''-diphenylindol-7''-yl)indol-2'yl]2,3-diphenylindole (19)

(0.31g, 45%), $R_f 0.75$, m.p. 180-186 °C. (Found: C, 79.6; H, 5.7; N, 4.4. $C_{60}H_{49}N_3O_6$ requires C, 79.4; H, 5.4; N, 4.6%). λ_{max} 244nm(ϵ 59630), 321(29960). v_{max} 3445, 1599, 1464, 1331,1139, 993, 697 cm⁻¹. ¹H n.m.r. (CDCl₃): δ 3.64, 3.72, 3.80, 3.84, 3.91 and 3.94, 6s, OMe; 6.30, 6.48 and 6.59, 3s, H5, H5' and H5"; 6.92-6.96, m, 2H, ArH; 7.16-7.37, m, 19H, ArH; 7.46-7.49, m, 2H, ArH; 7.61-7.63, m, 2H, ArH; 7.84, 8.06 and 8.36, 3s, NH. ¹³C n.m.r. (CDCl₃): δ 55.24, 55.41, 57.07, 57.72 and 57.80, OMe; 89.99, 90.35 and 90.84, C5, C5' and C5"; 125.83, 126.76, 126.87, 127.19, 127.29, 127.62, 127.84, 128.05, 128.32, 130.34, 131.41 and 131.51, ArCH; 97.98, 98.51 and 98.70, C3, C3' and C3"; 111.97, 113.18, 113.51, 113.95, 114.89 and 115.31, C3a, C3'a, C3"a, C7a, C7'a and C7"a; 132.53, 132.63, 132.75, 132.98, 135.55, 135.83, 136.12, 136.97 and 137.38, ArC; 154.15, 154.34, 154.49, 154.76, and 155.05, <u>C</u>-OMe. Mass spectrum: *m/z* 909(M+2, 25%), 908(M+1, 65), 907(M, 100).

(ii) 2,2'-Bi-(4,6-dimethoxy-3-phenyl)indolyi (21)

(0.02g, 1.5%), $R_f 0.65$, m.p. 275-279 °C. (Found: C, 76.2; H, 5.8; N, 5.5. $C_{32}H_{28}N_2O_4$ requires C, 76.2; H, 5.6; N, 5.6%). λ_{max} 230nm(ϵ 43570), 278(23570), 330(12860). ν_{max} 3368, 1619, 1519, 1462, 1377, 1314, 1199, 1133, 899 cm⁻¹. ¹H n.m.r. [(CD₃)₂SO]: δ 3.60 and 3.76, 2s, OMe; 6.14, d, J2.0Hz, H5, H5'; 6.43, d, J2.0Hz, H7, H7'; 6.94-7.03, m, ArH; 11.28, s, NH. ¹³C n.m.r. [(CD₃)₂SO]: δ 55.06 and 55.47, OMe; 87.00, C5; 91.92, C7; 125.05, 126.75 and 130.48, ArCH; 110.93, 116.95, 135.81, 137.63 and 137.78, ArC; 154.41 and 157.04, <u>C</u>-OMe. Mass spectrum: *m/z* 505(M+1, 10%), 504(M, 30), 489(10), 252(15), 149(30).

Reaction of indole 1 and indolin-2-one 11 with triflic anhydride

Indole 1 (0.5g, 1.52mmol) and indolin-2-one 11 (0.41g, 1.53mmol) gave the terindolyl 19 (0.41g, 60%), R_f 0.75, m.p. 180-186 °C.

Reaction of indole 1 and indolin-2-one 13 with phosphoryl chloride

Indole 1 (0.5g, 1.52mmol) and indolin-2-one 13 (0.32g, 1.54mmol) gave 4,6-dimethoxy-7-[4',6'-dimethoxy-3'-methyl-7'-(4'',6''-dimethoxy-2'',3''-diphenylindol-7''-yl)indol-2'-yl]2,3-diphenylindole 20 (0.32g, 50%) m.p. 142-144 °C. (Found: C, 77.8; H, 5.9; N, 4.7. C₅₅H₄₇N₃O₆ requires C,78.1; H, 5.6; N, 5.0%). λ_{max} 245nm(ϵ 59300), 324(28270). ν_{max} 3419, 1599, 1457, 1377, 1328, 1258, 1204, 1138, 996 cm⁻¹. ¹H n.m.r. (CDCl₃): δ 2.45, s, Me; 3.65, 3.85 and 4.05, 3s, OMe; 3.70, s, 9H, OMe; 6.40, 6.45 and 6.50, 3s, H5, H5' and H5"; 7.20-7.45, 20H, ArH; 7.85, 8.05 and 8.20, 3s, NH. ¹³C n.m.r. (CDCl₃): δ 12.29, Me; 55.45, 57.00 and 57.91, OMe; 89.60, 89.98 and 91.11, C5, C5' and C5"; 125.80, 125.92, 126.84, 127.04, 127.26, 127.31, 128.05, 128.30, 128.35, 131.45 and 131.51, ArCH; 97.61, 98.84 and 99.23, C3, C3' and C3"; 110.29, 113.01, 113.62, 114.18, 114.84 and 114.88, C3a, C3'a, C3'a, C7a, C7'a and C7"a; 132.73, 132.75, 132.79, 133.04, 135.86, 136.15, 136.93 and 137.47, ArC; 153.97, 154.23, 154.69, 154.75, 155.01 and 155.09, <u>C</u>-OMe. Mass spectrum: *m*/z 847(M+2, 20%), 846(M+1, 65), 845(M, 100), 830(15), 656(20), 532(20).

Reaction of indole 1 and indolin-2-one 13 with triflic anhydride

Indole 1 (0.5g, 1.52mmol) and indolin-2-one 13 (0.32g, 1.54mmol) gave the terindolyl 20 (0.32g, 50%) m.p. 142-144 °C.

5,7-Dimethoxy-8-(4',6'-dimethoxy-2',3'-diphenylindol-7'-yl)-1,4-dithia-1,2,3,4-tetrahydrocarbazole (23) Reaction of indole 1 (0.5g, 1.52mmol) and indolin-2-one 14 (0.43g, 1.52 mmol) with phosphoryl chloride (0.28ml, 3.04mmol) after 6h reflux gave the biindolyl 23 (0.45g, 50%), m.p. 258-260 °C (from dichloromethane and petroleum ether). (Found: C, 68.8; H, 5.0; N, 4.9. C₃₄H₃₀N₂04S₂ requires C, 68.7; H, 5.1; N, 4.7%). λ_{max} 248nm(ϵ 35892), 319(20649). ν_{max} 3463, 3373, 1594, 1507, 1329, 1206, 1140, 994, 699 cm⁻¹. ¹H n.m.r. [(CD₃)₂SO]: δ 3.20-3.35, m, CH₂; 3.66, 3.68, 3.70 and 3.88, 4s, OMe; 6.40 and 6.46, 2s, H6 and H5'; 7.14-7.26, m, ArH; 10.25, s, NH; 10.31, s, NH. ¹³C n.m.r. [(CD₃)₂SO]: δ 26.81 and 27.56, CH₂; 55.44, 57.73, 56.82 and 56.88, OMe; 89.65 and 90.56, C5 and C5'; 125.79, 126.79, 127.42, 127.94, 129.26 and 131.53, ArCH; 96.58, 99.26, 99.51, 111.96, 112.74, 113.78, 118.17, 132.92, 133.24, 136.89, 137.20 and 137.86, ArC; 151.91, 153.90, 154.10 and 154.43, <u>C</u>OMe. Mass spectrum: *m*/z 597(M+2, 20%), 596(M+1, 40%), 595(M, 100%), 567(25).

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